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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/454,740	12/06/1999	TIMO HILLEBRAND	2936.166/00	4186

7590 07/10/2002

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 07/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/454,740	Applicant(s) HILLEBRAND ET AL.	
	Examiner Arun Chakrabarti	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11 and 26-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on May 31, 2002 for a Continued Prosecution Application (CPA) under 37 CAR 1.53(d) based on parent Application No. 09/454,740 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-5, 7, 9 and 26-29 are rejected under 35 U.S.C. 103(a) over Anderson et al. (U.S. Patent 5,948,656) (September 7, 1999) in view of Cleuziat et al. (U.S. Patent 5,824,517) (October 20, 1998) further in view of Nochumson et al. (U.S. Patent 5,552,325) (September 3, 1996) further in view of Gonsalves et al. (U.S. Patent 5,907,085) (May 25, 1999) further in view of Asgari et al. (U.S. Patent 5,858,649) (January 12, 1999).

Anderson et al. teach formulations without chaotropic components for isolating nucleic acids (Example I), in particular of DNA, from optional complex starting materials consisting essentially of:

- a lysis/binding buffer system which contains a salt component (Example I, column 15, lines 23-24),

- wash and elution buffers (Example I, column 15, lines 27-32).

Anderson et al. teach the formulations wherein the lysis/binding buffer system contain detergents and additive (Example I, column 15, line 24).

Anderson et al. teach the formulations wherein the detergents are Tris-HCl, EDTA, SDS and triton X-100 (Example I, column 15, lines 24-25).

Anderson et al. teach the formulations wherein the lysis/binding buffer system contains an alcohol (Example I, column 15, lines 25-26).

Anderson et al do not teach the binding of nucleic acid to a substrate.

Cleuziat et al. teach the binding of nucleic acid to a substrate (Column 5, line 49 to column 6, line 24).

Anderson et al do not teach the complex starting material chosen from the group consisting of compact plant materials, whole blood, tissue, foodstuffs and other sources suspected of containing biological organisms.

Cleuziat et al. teach the complex starting material chosen from the group consisting of compact plant materials, whole blood, tissue, foodstuffs and other sources suspected of containing biological organisms (Column 8, lines 47-54).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the solid substrate of Cleuziat et al. in the lysing buffer of Anderson et al., since Cleuziat et al. state, "The term solid substrate as used here includes all materials on which a nucleic acid fragment can be immobilized for utilization in diagnostic tests, in affinity chromatography, and in separation processes (Column 5, lines 49-52)". An ordinary practitioner would have been motivated to combine and substitute the solid substrate of Cleuziat et al. in the lysing buffer of Anderson et al. in order to achieve the express advantage of a system, as noted by Cleuziat et al, on which a nucleic acid fragment can be immobilized for utilization in diagnostic tests, in affinity chromatography, and in separation processes.

Anderson et al in view of Cleuziat et al do not teach a wash buffer comprising at least 50% ethanol, and a low elution buffer.

Nochumson et al teach a wash buffer comprising at least 50% ethanol, and a low salt elution buffer.(Column 12, lines 34-58 and Examples 1 and 3, Column 13 and 14 respectively).

Anderson et al in view of Cleuziat et al do not teach the elution buffer comprising Tris-HCl, TE, and water.

Nochumson et al teach the elution buffer comprising Tris-Hcl, TE, and water (Column 12, lines 34-58).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the wash and elution buffer of Nochumson et al. in the nucleic acid isolating system of Anderson et al in view of Cleuziat et al since Nochumson et al. state, "It is important to maintain a high enough ionic strength to avoid washing off bound DNA (Column 12, lines 39-41)". An ordinary practitioner would have been motivated to combine and substitute the wash and elution buffer of Nochumson et al. in the nucleic acid isolating system of Anderson et al in view of Cleuziat et al. in order to achieve the express advantage of a buffer system, as noted by Nochumson et al, which avoid washing off bound DNA by the wash buffer and enhances elution at a low ionic strength.

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. do not teach the lysis/binding buffer system containing enzymes degrading proteins in aqueous solution.

Gonsalves et al teach the lysis/binding buffer system containing enzymes degrading proteins in aqueous solution (Example I, column 35, lines 34-36 and Example 12, column 43, lines 43-49).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the proteinase K of Gonsalves et al. in the

nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al., since Gonsalves et al. states, "Samples prepared with proteinase K-treated crude extract have an advantage over others in that hazardous organic solvents, such as phenol and chloroform, are avoided (Column 43, lines 46-49)". An ordinary practitioner would have been motivated to combine and substitute the proteinase K of Gonsalves et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al., in order to achieve the express advantage of a system, as noted by Gonsalves et al, which has advantage over others in that hazardous organic solvents, such as phenol and chloroform, are avoided.

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. do not teach the antichaotropic component ammonium chloride.

Asgari et al teach the antichaotropic component ammonium chloride (Column 9, lines 47-50).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine ammonium chloride as a lysing reagent of Asgari et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al., since Asgari et al. state, "A preliminary step involving lysis of maternal erythrocytes involving, e.g., with ammonium chloride, can conveniently be used to remove a substantial proportion of these red cells (Column 9, lines 47-50)". An ordinary practitioner would have been motivated to substitute the

ammonium chloride of Asgari et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. in order to achieve the express advantage of a system, as noted by Asgari et al, which can conveniently be used to remove a substantial proportion of red cells from erythrocytes to selectively purify white blood cells.

4. Claim 8 is rejected under 35 U.S.C. 103 (a) over Anderson et al. (U.S. Patent 5,948,656) (September 7, 1999) in view of Cleuziat et al. (U.S. Patent 5,824,517) (October 20, 1998) further in view of Nochumson et al. (U.S. Patent 5,552,325) (September 3, 1996) further in view of Gonsalves et al. (U.S. Patent 5,907,085) (May 25, 1999) further in view of Asgari et al. (U.S. Patent 5,858,649) (January 12, 1999) further in view of Summerton et al. (U.S. Patent 6,060,246) (May 9, 2000).

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. further in view of Asgari et al. teach the formulations of claims 1-5, 7, 9 and 27-29 as described above

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Asgari et al. do not teach the formulations wherein the buffer system is a solid formulation stable in storage in reaction vessel ready for use.

Summerton et al teach the formulations wherein the buffer system is a solid formulation stable in storage in reaction vessel ready for use (Column 10, lines 52-57).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute dried buffer of Summerton et al in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. further in view of Asgari et al., since Summerton et al. state, "This pH adjustment can be readily carried out as part of the specimen preparation step, simply by incorporating in the specimen receiving container a suitable buffer, preferably in dry form, effective to adjust the specimen to the proper pH for electrostatic capture of polynucleotides (Column 10, lines 52-57)". An ordinary practitioner would have been motivated to substitute dried buffer of Summerton et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. further in view of Asgari et al., in order to achieve the express advantage of a system, as noted by Summerton et al, which provides effective adjustment of the specimen to the proper pH for electrostatic capture of polynucleotides .

5. Claims 10 and 11 are rejected under 35 U.S.C. 103 (a) over Anderson et al. (U.S. Patent 5,948,656) (September 7, 1999) in view of Cleuziat et al. (U.S. Patent 5,824,517) (October 20, 1998) further in view of Nochumson et al. (U.S. Patent 5,552,325) (September 3, 1996) further in view of Gonsalves et al. (U.S. Patent 5,907,085) (May 25, 1999) further in view of Asgari et al. (U.S. Patent 5,858,649) (January 12, 1999) further in view of Woodard et al. (U.S. Patent 5,650,506) (July 12, 1997).

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Asgari et al. teach the formulations of claims 1-5, 7, 9 and 27-29 as described above

Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. further in view of Asgari et al. do not teach the formulations wherein all carriers which have a negatively functionalised surface or functionalised surfaces which may be converted to a negative charge potential serve as solid phase and wherein the surface of the carrier is modified by a hydroxyl group.

Woodard et al teach the formulations wherein all carriers which have a negatively functionalised surface or functionalised surfaces which may be converted to a negative charge potential serve as solid phase and wherein the surface of the carrier is modified by a hydroxyl group (Abstract and Column 2, lines 40-57 and column 4, lines 44-54).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the negatively charged surface containing solid phase of Woodard et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al. further in view of Asgari et al., since Woodard et al. state, "The modified glass fiber membranes of the present invention allows very quick and efficient isolation of DNA from biological samples. They can substantially decrease the time required to process pure DNA from biological samples, compared with currently used techniques, and in some cases generate high quantities of pure DNA (Column 4, lines 44-49)". An ordinary practitioner would have been motivated to substitute the negatively

charged surface containing solid phase of Woodard et al. in the nucleic acid isolation method of Anderson et al. in view of Cleuziat et al. further in view of Nochumson et al. further in view of Gonsalves et al., in order to achieve the express advantage of a system, as noted by Woodard et al, which allows very quick and efficient isolation of DNA from biological samples and in some cases generate high quantities of pure DNA .

Response to Arguments

6. Applicant's arguments filed on 1/11/02 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Gonsalves et al as Gonsalves et al. states, "Samples prepared with proteinase K-treated crude extract have an advantage over others in that hazardous organic solvents, such as phenol and chloroform, are avoided (Column 43, lines 46-49)". Moreover, strong motivations are further provided by Woodard et al since Woodard et al. state, "The modified glass fiber membranes of the present invention allows very quick and efficient

isolation of DNA from biological samples. They can substantially decrease the time required to process pure DNA from biological samples, compared with currently used techniques, and in some cases generate high quantities of pure DNA (Column 4, lines 44-49)". Similar strong motivations are provided by Cleuziat et al., Nochumson et al., and Asgari et al.

In response to applicant's argument that antichaotropic agents in the cited prior arts are used as binding DNA to substrate whereas the instant invention uses antichaotropic agents as releasing DNA from the substrate or ammonium chloride of Asgari reference is not used as antichaotropic agent, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Applicant then argues the 103 rejection is improper because it lacks a reasonable expectation of success.

With regard to the lack of reasonable expectation of success argument, The MPEP 2143.02 states

"Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA

1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Gonsalves reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different enzymes were actually experimentally studied and found to be functional to prepare samples with proteinase K-treated crude extract, which has an advantage over others in that hazardous organic solvents, such as phenol and chloroform, are avoided (Column 43, lines 46-49). This evidence of

functionality trumps the attorney arguments, which argues that Gonsalves reference is an invitation to research, since Gonsalves steps beyond research and shows the functional product.

Applicant argues that Anderson reference does not teach the antichaotropic reagents of the claimed invention. Applicant argues that the word "antichaotropes" was not found in Anderson reference. Applicant's argument is moot in view of the new grounds of 103 (a) rejection (as mentioned in Section 4) based on the same prior art.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

June 24, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600